Dual action of liraglutide and insulin degludec in type 2 diabetes: A trial comparing the efficacy and safety of insulin degludec/liraglutide, insulin degludec and liraglutide in subjects with type 2 diabetes

This trial is conducted globally. The aim of this trial is to compare the efficacy and safety of insulin degludec/liraglutide (IDegLira) versus insulin degludec (IDeg) and liraglutide (Lira) in subjects with type 2 diabetes. Subjects are to continue their pre-trial treatment with metformin or metformin + pioglitazone throughout the entire trial.

Scientific Title
A 26 week randomised, parallel three-arm, open-label, multi-centre, multinational treat-to-target trial comparing fixed ratio combination of insulin degludec and liraglutide versus insulin degludec or liraglutide alone, in subjects with type 2 diabetes treated with 1-2 oral anti-diabetic drugs (OADs) with a 26 week extension

<table>
<thead>
<tr>
<th>Trial IDs and acronym(s)</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novo Nordisk Trial ID</td>
<td>Diabetes</td>
</tr>
<tr>
<td>NN9068-3697</td>
<td>Diabetes Mellitus, Type 2</td>
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<tr>
<td>Clinical Trials.gov Registration</td>
<td>Trial phase</td>
</tr>
<tr>
<td>NCT01336023</td>
<td>Phase 3</td>
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<td>Other Identifier(s)</td>
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<td>EudraCT Number: 2010-021560-15</td>
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<td>Other Identifier: U1111-1119-1174</td>
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<td>DUAL™ I</td>
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</table>

<table>
<thead>
<tr>
<th>Trial dates</th>
<th>Arm Information with Assigned Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start date: 23.May.2011</td>
<td>No. of arms: 3</td>
</tr>
<tr>
<td>Primary completion date: 24.May.2012</td>
<td>IDeg (Experimental):</td>
</tr>
<tr>
<td>Completion date: 22.Nov.2012</td>
<td>Arm description:</td>
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- insulin degludec/liraglutide
- insulin degludec
- liraglutide

Drug: insulin degludec

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Insulin degludec treatment will be initiated with 10 U and titrated (individually adjusted) twice weekly according to the mean SMPG (fasting). Insulin degludec is injected subcutaneously (under the skin) once daily.

- **IDEgLira (Experimental):**
  - Arm description:
    - Drug: insulin degludec/liraglutide
    Insulin degludec/liraglutide treatment will be initiated and titrated (individually adjusted) twice weekly according to the mean self measured plasma glucose (SMPG) (fasting). Insulin degludec/liraglutide is injected subcutaneously (under the skin) once daily.

- **Lira (Experimental):**
  - Arm description:
    - Drug: liraglutide
    Liraglutide will be started with 0.6 mg and subsequent 0.6 mg weekly dose escalation to 1.8 mg. Liraglutide dose of 1.8 mg/day will be continued for the remaining part of the trial. Liraglutide is injected subcutaneously (under the skin) once daily.

<table>
<thead>
<tr>
<th>Trial status</th>
<th>No. of trial participants</th>
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<tbody>
<tr>
<td>Completed</td>
<td>1663</td>
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<table>
<thead>
<tr>
<th>Age eligible for trial participation</th>
<th>Genders eligible for trial participation</th>
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<tbody>
<tr>
<td>18 years and above</td>
<td>Both</td>
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<thead>
<tr>
<th>Inclusion criteria</th>
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<tbody>
<tr>
<td>- Subjects with type 2 diabetes</td>
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<tr>
<td>- HbA1c 7.0-10.0 % (both inclusive) with the aim of a median HbA1c of 8.3%.</td>
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<tr>
<td>Accordingly, when approximately 50% of the randomised subjects have a HbA1c above 8.3%, the remaining subjects randomised must have a HbA1c of below or equal to 8.3%, or when approximately 50% of the randomised subjects have a HbA1c of below or equal to 8.3%, the remaining subjects randomised must have a HbA1c above 8.3%</td>
</tr>
<tr>
<td>- Male or female, age 18 years or above</td>
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<tr>
<td>(Taiwan: 20 years or above for a site 653 in Taiwan: Taichung Veterans General Hospital)</td>
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<tr>
<td>- Subjects on stable dose of 1-2 OADs (metformin [at least 1500 mg or max tolerated dose] or metformin [at least 1500 mg or max tolerated dose] + pioglitazone [at least 30 mg]) for at least 90 days prior</td>
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<table>
<thead>
<tr>
<th>Exclusion criteria</th>
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<tbody>
<tr>
<td>- Treatment with insulin (except for short-term treatment due to intercurrent illness at the discretion of the Investigator)</td>
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<tr>
<td>- Treatment with GLP-1 (glucagon-like peptide-1) receptor agonists (eg exenatide, liraglutide), sulphonylurea or dipeptidyl peptidase 4 (DPP-4) inhibitors within 90 days prior to trial</td>
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<tr>
<td>- Impaired liver function, defined as alanine aminotransferase (ALAT) at least 2.5 times Upper Normal Range (UNR) (one retest analysed at the central laboratory within a week from first sample taken is permitted with the result of the last sample being the conclusive)</td>
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<tr>
<td>- Impaired renal function defined as serum-creatinine at least 133 mcmol/l (at least 1.5 mg/dl) for males and at least 125 mcmol/l (at least 1.4) for females, or as allowed according to local contraindications for</td>
</tr>
</tbody>
</table>

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to screening
- Body Mass Index (BMI) maximum 40 kg/m^2
- metformin (one retest analysed at the central laboratory within a week from first sample taken is permitted with the result of the last sample being the conclusive)
- Screening calcitonin at least 50 ng/L
- Subjects with personal or family history of medullary thyroid carcinoma (MTC) or multiple endocrine neoplasia type 2 (MEN 2)
- Cardiac disorder defined as: congestive heart failure (NYHA class III-IV), diagnosis of unstable angina pectoris, cerebral stroke and/or myocardial infarction within the last 12 months and planned coronary, carotid or peripheral artery revascularisation procedures
- Severe uncontrolled treated or untreated hypertension (systolic blood pressure at least 180 mm Hg or diastolic blood pressure at least 100 mm Hg)
- Acute treatment required proliferative retinopathy or maculopathy (macular oedema)
- History of chronic pancreatitis or idiopathic acute pancreatitis

**Trial type**
**Interventional**

**Trial design**
Purpose: Treatment
Allocation: Randomized
Masking:
Control: Active Control
Assignment: Parallel Assignment

**Primary outcome**
- Mean change from baseline in HbA1c (glycosylated haemoglobin) at week 26
  Time frame: Week 0, week 26

**Secondary outcome(s)**
- Mean change from baseline in body weight at week 26
  Time frame: Week 0, Week 26
- Number of hypoglycaemic episodes
  Time frame: Weeks 0-26
- Change from baseline in incremental area under the curve 0-4h (iAUC0-4h) derived from the glucose concentration profile during meal test
  Time frame: Week 0, Week 26
- Mean actual daily insulin dose
  Time frame: Week 26

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Participating countries
Australia: Completed/Suspended
Canada: Completed
Finland: Completed
Germany: Completed/Suspended
Hungary: Completed/Suspended
India: Completed
Ireland: Completed
Italy: Completed/Suspended
Malaysia: Completed/Suspended
Mexico: Completed
Russian Federation: Completed/Suspended
Singapore: Completed
Slovakia: Completed
South Africa: Completed/Suspended
Spain: Completed
Taiwan: Completed/Suspended
Thailand: Completed
United Kingdom: Completed
United States: Completed/Suspended

Central contact information
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For trials conducted in the US: (+1) 866-867-7178

Labeling information
• EU:

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